Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	OCT 23	The Derwent World Patents Index suite of databases on STN has been enhanced and reloaded
NEWS 4	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 5	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 6	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 7	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 8	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 9	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 10	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 11	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 12	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 13	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 14	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 15	DEC 18	CA/CAplus patent kind codes updated
NEWS 16	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 17	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 18	DEC 27	CA/CAplus enhanced with more pre-1907 records
NEWS 19	JAN 08	CHEMLIST enhanced with New Zealand Inventory of Chemicals
NEWS 20	JAN 16	CA/CAplus Company Name Thesaurus enhanced and reloaded
NEWS 21	JAN 16	IPC version 2007.01 thesaurus available on STN
NEWS 22	JAN 16	WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data

NEWS EXPRESS	NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8
NEWS X25	X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific

* * * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 11:27:50 ON 19 JAN 2007

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 11:28:04 ON 19 JAN 2007

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 JAN 2007 HIGHEST RN 917745-84-7
DICTIONARY FILE UPDATES: 17 JAN 2007 HIGHEST RN 917745-84-7

New CAS Information Use Policies, enter HELP USAGETERMS for details.

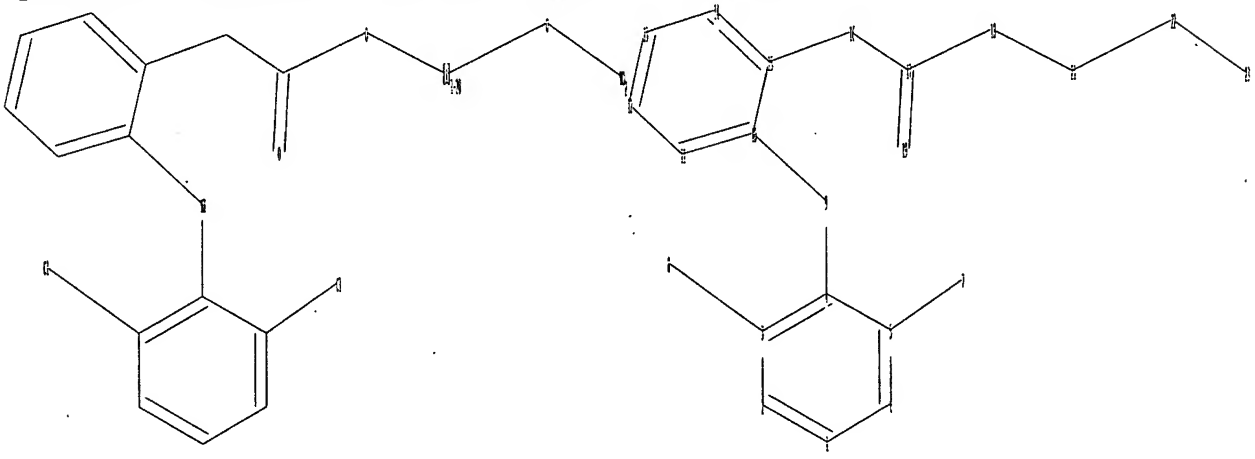
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=>
Uploading C:\Program Files\Stnexp\Queries\10527647\Struc 1.str



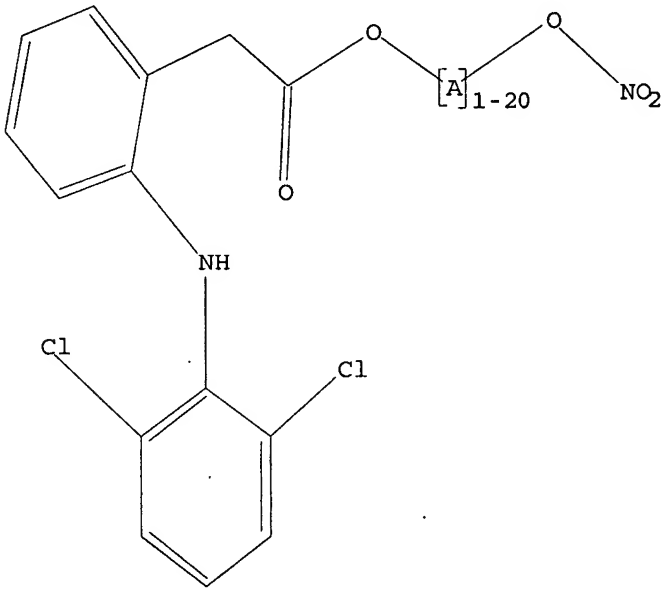
chain nodes :
7 8 9 16 17 18 19 21 22 23
ring nodes :
1 2 3 4 5 6 10 11 12 13 14 15
chain bonds :
3-8 4-9 5-7 9-10 15-16 16-17 17-18 17-19 18-21 21-22 22-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15
exact/norm bonds :
4-9 9-10 17-18 17-19 18-21 21-22 22-23
exact bonds :
3-8 5-7 15-16 16-17
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 10-11 10-15 11-12 12-13 13-14 14-15

G1:C,O

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS 19:CLASS
21:CLASS 22:CLASS 23:CLASS

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 C,O

Structure attributes must be viewed using STN Express query preparation.

```
=> l1
SAMPLE SEARCH INITIATED 11:28:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -        3 TO ITERATE

100.0% PROCESSED         3 ITERATIONS                                  3 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:             3 TO      163
PROJECTED ANSWERS:                3 TO      163

L2             3 SEA SSS SAM L1

=> l1 full
FULL SEARCH INITIATED 11:28:53 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -       45 TO ITERATE

100.0% PROCESSED        45 ITERATIONS                                 14 ANSWERS
SEARCH TIME: 00.00.01

L3            14 SEA SSS FUL L1

=> file medline caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   172.55     172.76

FILE 'MEDLINE' ENTERED AT 11:29:28 ON 19 JAN 2007

FILE 'CAPLUS' ENTERED AT 11:29:28 ON 19 JAN 2007
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2007 AMERICAN CHEMICAL SOCIETY (ACS)

=> l3
L4            41 L3

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5             33 DUP REM L4 (8 DUPLICATES REMOVED)

=> d ibib abs hitstr 1-33
```

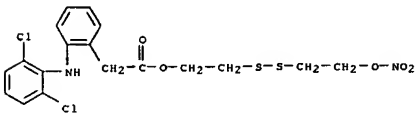
L5 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:191976 CAPLUS
DOCUMENT NUMBER: 144:273755
TITLE: Preparation of prodrugs containing novel biocleavable linkers
INVENTOR(S): Satyam, Apparao
PATENT ASSIGNEE(S): Nicholas Piramal India Ltd., India
SOURCE: U.S. Pat. Appl. Publ., 181 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006046967	A1	20060302	US 2005-213396	20050826
US 2006205674	A2	20060914		
WO 2006027711	A2	20060316	WO 2005-IB52797	20050826
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-604632P P 20040826
IN 2005-MU779 A 20050701

OTHER SOURCE(S): MARPAT 144:273755
AB The invention provides compds. D1-L1-E-A-B-A1-E-(L-E-A1-B-A-E)0-2-L2-D2 [B is a bond, (CH2)1-6, (CH2CH2O)1-1000, S-S, S-S:O, S-SO2 or S-S:NH; A, A1 are independently a bond, (CH2)1-8, 1,2-, 1,3- or 1,4-phenylene; D1 is a therapeutic agent having one or more functional groups OH, SH, NHR1, CO2H, CONHR1, O2CNHR1, SO2NHR1, SO2NHR1, NR1CONHNHR1 or NR1SO2NHR1 (R1 is H, alkyl, aryl, etc.); D2 is D1, a peptide, protein, monoclonal antibody, vitamin, NO, NO2, NONOate, a nitric oxide-releasing group, a polymer, etc.; E is independently CH2 or a bond; L1, L2 are independently a bond, O, S, NR1, L, or a linkage] or their pharmaceutically-acceptable salts for use as prodrugs, including NO-releasing prodrugs. Thus, aspirin prodrug 2-AcOC6H4CONHCH2CH2SSCH2CH2ONO2 was prepared and shown to release salicylate in rats in a sustained and controlled manner starting from 1 h through 12 h.
IT 877865-14-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

L5 ANSWER 1 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(Uses)
(prepn. of prodrugs contg. novel biocleavable linkers)
RN 877865-14-0 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[[2-(nitrooxy)ethyl]dithio]ethyl ester (9CI) (CA INDEX NAME)

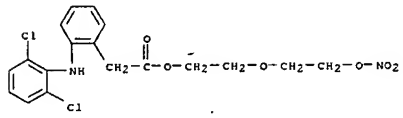


L5 ANSWER 2 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1154582 CAPLUS
DOCUMENT NUMBER: 142:100367
TITLE: Pharmaceutical compositions based on diclofenac derivative
INVENTOR(S): Gustafsson, Christina; Kjellberg, Ulf; Morein, Sven
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004112753	A1	20041229	WO 2004-SE1017	20040623
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2529963	A1	20041229	CA 2004-2529963	20040623
EP 1635790	A1	20060322	EP 2004-749055	20040623
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2006141044	A1	20060629	US 2005-560824	20051215

PRIORITY APPLN. INFO.: SE 2003-1880 A 20030625
WO 2004-SE1017 W 20040623

AB The present invention relates to particles comprising the NO-donating diclofenac derivative, 2-[2-(nitrooxy)ethoxy]ethyl (2-[(2,6-dichlorophenyl)amino]phenyl)acetate (I), optionally mixed with one or more surfactant(s) and to a new drug delivery composition comprising said particles optionally in combination with a second drug. Furthermore, the invention relates to processes for preparing said particles and drug delivery composition as well as the use of said composition in the manufacturing of a medicament. For example, 10.5 g I and 29.5 g Pearlitol 100 SD were mixed and the mixture was heated to 75° until the drug was fully melted. The mixture was cooled to room temperature and the powder obtained was sieved through a 0.355 mm sieve. The sieved powder (37.8 g) was mixed with 0.62 g microcryst. cellulose, 0.63 g Polyvidon XL, and 0.41 g Polyvidon K-30, and the powder was wet-granulated. The granulate was dried overnight at 45°, 0.38 g collodial silica was added and the powder was mixed. Sodium stearyl fumarate (0.20 g) was added to the mixture followed by mixing. The granulate was filled into hard gelatin capsules. The drug release from capsules was 12.1%, 33.4%, 60.7%, 79.6% and 88.14% in 5, 10, 20, 45, and 90 min, resp.
IT 174454-43-4
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES
(Uses)
(porous particle compns. comprising NO-donating diclofenac derivative)
RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



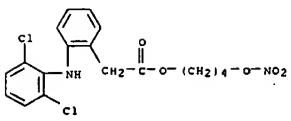
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:354783 CAPLUS
DOCUMENT NUMBER: 140:350593
TITLE: Use of NO-donating NSAIDs for the treatment of conditions associated with gastrointestinal motility
INVENTOR(S): Jonzon, Bror; Hoogstraate, Janet
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035042	A1	20040429	WO 2003-SE1603	20031015
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003269774	A1	20040504	AU 2003-269774	20031015
PRIORITY APPLN. INFO.:			SE 2002-3093	A 20021018
			WO 2003-SE1603	W 20031015

OTHER SOURCE(S): MARPAT 140:350593
AB The invention discloses the use of NO-donating nonsteroidal antiinflammatory drugs in the treatment of conditions associated with gastrointestinal motility, a method of treatment of such conditions, and the use of pharmaceutical compns. comprising one or more NO-donating NSAID(s) in the treatment of such conditions. More particularly, the invention is directed to the use of one or more NO-donating NSAID(s) for the manufacture of a medicament for the treatment of conditions associated with
disturbed gastrointestinal motility.
IT 156661-01-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NO-donating NSAIDs for treatment of conditions associated with gastrointestinal motility)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 3 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



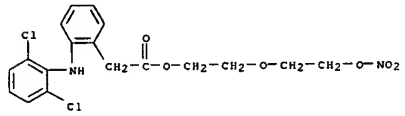
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:267282 CAPLUS
DOCUMENT NUMBER: 140:287165
TITLE: Manufacturing process for NO-donating compounds such as NO-donating diclofenac
INVENTOR(S): Andersson, Johan; Belli, Aldo; Cannata, Vincenzo; Hedberg, Martin; Palmgren, Andreas; Schuldei, Sigrid; Stroem, Marika; Villa, Marco
PATENT ASSIGNEE(S): Astrazeneca UK Limited, UK; Astrazeneca AB
SOURCE: PCT Int. Appl., 68 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

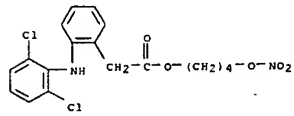
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004026808	A1	20040401	WO 2003-SE1465	20030918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498943	A1	20040401	CA 2003-2498943	20030918
AU 2003265035	A1	20040408	AU 2003-265035	20030918
BR 2003014365	A	20050719	BR 2003-14365	20030918
EP 1558559	A1	20050803	EP 2003-797782	20030918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1684940	A	20051019	CN 2003-822285	20030918
JP 2006500409	T	20060105	JP 2004-538109	20030918
ZA 2005002224	A	20060222	ZA 2005-2224	20050316
US 2006122402	A1	20060608	US 2005-527647	20050801
PRIORITY APPLN. INFO.:			SE 2002-2801	A 20020920
			SE 2003-1476	A 20030520
			WO 2003-SE1465	W 20030918

OTHER SOURCE(S): CASREACT 140:287165; MARPAT 140:287165
AB NO-Donating compds. MLnAmCO2XONOp [M = residue of an NSAID, COX-1 inhibitor or COX-2 inhibitor; L = O, S, CO2, (un)substituted CONH, NH, CO,
CH2, CH2CO, CH2CONH, CH2CO2; A = (un)substituted alkylene; X = carbon linker; m, n = 0-3; p= 1, 2] are prepared by treating MLnAmCO2H with HOXOH,
treating MLnAmCO2XOH with RSO2Cl [R = alkyl, (un)substituted Ph, CH2Ph, halogen, CF3, C4F9], and treating MLnAmCO2XO3SR with nitrate. A substantially crystalline form of 2-[2-(nitrooxy)ethoxy]ethyl (2-[(2,6-dichlorophenyl)amino]phenyl)acetate is reported.
IT 174454-43-4P
RL: IMF (Industrial manufacture); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(manufacturing process for NO-donating compds. such as NO-donating

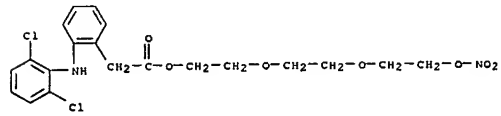
L5 ANSWER 4 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
diclofenac)
RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



IT 156661-01-7P 676125-87-4P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(manufacturing process for NO-donating compds. such as NO-donating diclofenac)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 676125-87-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-[2-(nitrooxy)ethoxy]ethoxy]ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:41217 CAPLUS
DOCUMENT NUMBER: 140:111135
TITLE: Preparation of nitrosated nonsteroidal antiinflammatory compounds
INVENTOR(S): Earl, Richard A.; Ezawa, Maiko; Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Khanapure, Subhash P.; Letts, Gordon L.; Lin, Chia-En; Ranatunge, Ramani R.; Richardson, Stewart K.; Schroeder, Joseph D.; Stevenson, Cheri A.; Wey, Shiow-Jyi
PATENT ASSIGNEE(S): Nitromed, Inc., USA
SOURCE: PCT Int. Appl., 145 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004648	A2	20040115	WO 2003-US21026	20030703
WO 2004004648	A3	20041028		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2491127	A1	20040115	CA 2003-2491127	20030703
AU 2003247792	A1	20040123	AU 2003-247792	20030703
US 2004024057	A1	20040205	US 2003-612014	20030703
US 7163958	B2	20070116		
EP 1539729	A2	20050615	EP 2003-763193	20030703
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005539089	T	20051222	JP 2004-562619	20030703
US 2005222243	A1	20051006	US 2005-134358	20050523

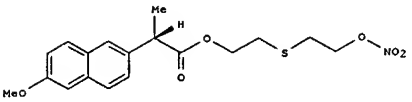
PRIORITY APPLN. INFO.:

US 2002-393111P	P	20020703
US 2002-397979P	P	20020724
US 2002-418353P	P	20021016
US 2003-449798P	P	20030226
US 2003-456182P	P	20030321
US 2003-612014	A3	20030703
WO 2003-US21026	W	20030703

OTHER SOURCE(S): MARPAT 140:111135

L5 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

GI

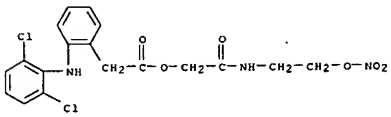


II

AB Title compds. RnRmHC-CO-X [Rm = H, alkyl; Rn = 4-{(thiophen-2-yl)carbonyl}phenyl, 3-(benzoyl)phenyl, etc.; X = Y-alkyl-aryl, etc.; Y = O, S; I] are prepared For instance, naproxen is coupled to 2,2'-thiodiethanol (CH2Cl2, DMAP, EDCI) and treated with Ac2O/HNO3 at 0° to give II. I are nitrosated nonsteroidal antiinflammatory drugs (NSAIDs) used alone or are combined with one compound that donates, transfers or releases nitric oxide, stimulates endogenous synthesis of nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor or is a substrate for nitric oxide synthase. The invention provides methods for treating inflammation, pain, fever, gastrointestinal disorders, etc.

IT 183195-09-7P, [N-[2-(Nitrooxy)ethyl]carbamoyl]methyl 2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetate 646511-34-4P, (2S)-2,3-Bis(nitrooxy)propyl 2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetate 646511-36-6P, (2R)-2,3-Bis(nitrooxy)propyl 2-[2-[(2,6-dichlorophenyl)amino]phenyl]acetate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naproxen-derived nitrosated antiinflammatory compds.)

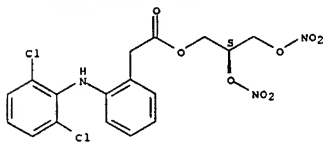
RN 183195-09-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[[2-(nitrooxy)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)



RN 646511-34-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, (2S)-2,3-bis(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

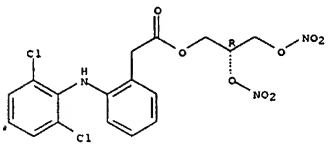
Absolute stereochemistry.

L5 ANSWER 5 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 646511-36-6 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, (2R)-2,3-bis(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

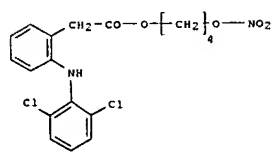
ACCESSION NUMBER: 2004:2666 CAPLUS
DOCUMENT NUMBER: 140:65191
TITLE: Oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having improved bioavailability
INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo; Macelloni, Cristina
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000273	A1	20031231	WO 2003-EP6496	20030620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI1392	A1	20031229	IT 2002-MI1392	20020625
CA 2491152	A1	20031231	CA 2003-2491152	20030620
AU 2003246564	A1	20040106	AU 2003-246564	20030620
EP 1526839	A1	20050504	EP 2003-760660	20030620
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
CN 1665486	A	20050907	CN 2003-815181	20030620
JP 2005530835	T	20051013	JP 2004-514802	20030620
NZ 537204	A	20060728	NZ 2003-537204	20030620
ZA 2004010109	A	20050902	ZA 2004-10109	20041214
NO 2005000347	A	20050121	NO 2005-347	20050121
US 2006171969	A1	20060803	US 2005-515621	20050912

PRIORITY APPLN. INFO.:

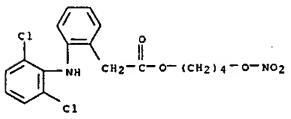
IT 2002-MI1392	A	20020625
WO 2003-EP6496	W	20030620

GI

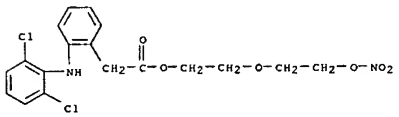


I

L5 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
AB The present invention relates to new pharmaceutical compns. for the administration of liquid drugs in solid oral forms, said compns. comprising one or more active ingredients, one or more surface-active agents and optionally a co-surfactant and/or an absorption enhancer absorbed on a solid inert carrier. An emulsion was prepared containing I 100, Cremophor EL 50, Phospholipon 80H 50, Aerosil 200 100, and Explotab 100 g.
IT 156661-01-7 174454-43-4 311336-64-8 311336-66-0 639067-68-8
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral pharmaceutical liquid drugs containing nitrate ester NSAIDs having improved bioavailability)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

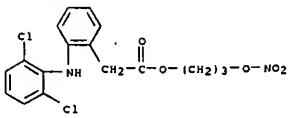


RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

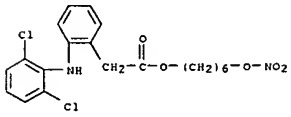


RN 311336-64-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)

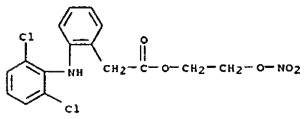
L5 ANSWER 6 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 311336-66-0 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 6-(nitrooxy)hexyl ester (9CI) (CA INDEX NAME)



RN 639067-68-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-(nitrooxy)ethyl ester (9CI) (CA INDEX NAME)



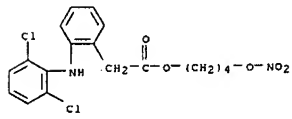
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:818296 CAPLUS
DOCUMENT NUMBER: 139:302040
TITLE: Nitrooxy derivatives of antiinflammatory/analgesic compounds for the treatment of arthritis
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

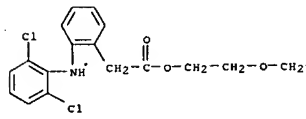
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084550	A1	20031016	WO 2003-EP3183	20030327
W: AE, AG, AL, AU, BA, BB, BR, BZ, CA, CN, CO, CR, CU, DM, DZ, EC, GD, GE, HR, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, SG, TN, TT, UA, US, UZ, VN, YU, ZA				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002MI0773	A1	20031013	IT 2002-MI773	20020411
AU 2003224002	A1	20031020	AU 2003-224002	20030327
EP 1492543	A1	20050105	EP 2003-720377	20030327
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005522472	T	20050728	JP 2003-581790	20030327
US 2007010458	A1	20070111	US 2006-509675	20060913
PRIORITY APPLN. INFO.:			IT 2002-MI773 A	20020411
			WO 2003-EP3183 W	20030327

OTHER SOURCE(S): MARPAT 139:302040
AB Antiinflammatory and/or antiinflammatory/analgesic compds. having the formula A(B)b0(C)c0-N(O)s [A contains radical of nonsteroidal antiinflammatory or nonsteroidal antiinflammatory/analgesic drug; B, C = bivalent linking group; s = 1, 2; b0, c0 = 0, 1 (with proviso)], and salts thereof, are disclosed for use in the treatment of arthritis.
IT 156661-01-7 174454-43-4
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy derivs. of antiinflammatory/analgesic compds. for treatment of arthritis)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 7 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



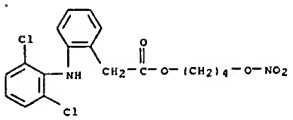
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:777566 CAPLUS
DOCUMENT NUMBER: 139:281272
TITLE: Nitric oxide-donating NSAIDS adsorbed into carrier particles
INVENTOR(S): Morein, Sven; Berg, Mats; Holmberg, Christina; Lundberg, Per Johan; Anders, Ringberg
PATENT ASSIGNEE(S): Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

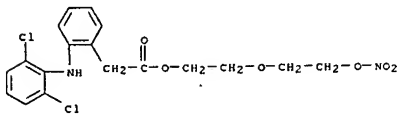
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080029	A1	20031002	WO 2003-SE468	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003216006	A1	20031008	AU 2003-216006	20030320
EP 1490033	A1	20041229	EP 2003-745055	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005129774	A1	20050616	US 2003-507368	20030320
JP 2005533751	T	20051110	JP 2003-577859	20030320
PRIORITY APPLN. INFO.:			SE 2002-895 A	20020322
			WO 2003-SE468 W	20030320

AB The present invention relates to porous particles comprising NO-donating nonsteroidal anti-inflammatory compound optionally mixed with surfactants and to new solid drug delivery composition comprising the particles optionally in combination with a second active drug. Furthermore, the invention relates to processes for producing the porous particles and solid drug delivery composition as well as the use of the composition in the manufacture of a medicament. The NO-donating NSAID may be in an oily or melted form. Thus, a tablet comprised 4-(nitrooxy)butyl (S)-2-(9-methoxy-2-naphthyl)propanoate (I) 250 and omeprazole 20 mg. Enteric over-coated pellets comprised omeprazole and a powder of the porous particles containing I were manufactured sep. before compressing the 2 components.
IT 156661-01-7 174454-43-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide-donating NSAIDS adsorbed into carrier particles)
RN 156661-01-7 CAPLUS

L5 ANSWER 8 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



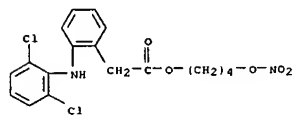
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:221490 CAPLUS
DOCUMENT NUMBER: 138:260440
TITLE: Self emulsifying drug delivery system containing NSAIDs
INVENTOR(S): Holmberg, Christina
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 49 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

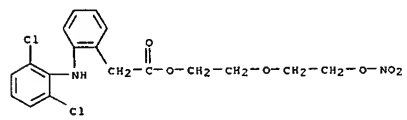
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003022249	A1	20030320	WO 2002-SE1598	20020905
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1427392	A1	20040616	EP 2002-765747	20020905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005504788	T	20050217	JP 2003-526379	20020905
US 2004248974	A1	20041209	US 2004-488585	20040304
PRIORITY APPLN. INFO.:			SE 2001-2993 A	20010907
			WO 2002-SE1598 W	20020905

OTHER SOURCE(S): MARPAT 138:260440
AB A pharmaceutical composition suitable for oral administration, in form of an emulsion pre-concentrate, comprises 1 or more NO-releasing NSAID(s), 1 or more surfactants, of which at least one is phospholipid, the composition forming an in-situ oil-in-water emulsion upon contact with gastrointestinal fluids. The composition may optionally also comprise an addnl. oil or semi-solid fat. Further, 1 or more short-chain alcs. can optionally be included in the composition Also within the scope of the invention is a combination with a proton pump inhibitor. The pharmaceutical composition is useful in the treatment of pain and inflammation. Further within the scope of the invention is kit comprising a pharmaceutical composition according to the invention in a unit dosage form, in combination with a proton pump inhibitor, and the proton pump inhibitor is enteric coated. Thus, a formulation contained Lipoid S100 0.30, propylene glycol 0.90, and a NO-releasing NSAID 4.00 g.
IT 156661-01-7 174454-43-4 311336-64-8
311336-66-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

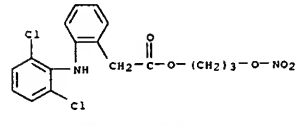
L5 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
(self emulsifying drug delivery system contg. NSAIDs)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

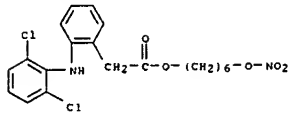


RN 311336-64-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)



RN 311336-66-0 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 6-(nitrooxy)hexyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 9 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

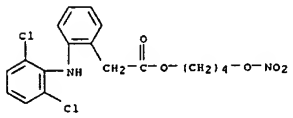
L5 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L5 ANSWER 10 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:133017 CAPLUS
DOCUMENT NUMBER: 138:163547
TITLE: Nitrooxy compounds for treatment of vasculopaties
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003013499	A2	20030220	WO 2002-EP8374		20020726
WO 2003013499	A3	20031231			
W: AE, AG, AL, AU, BA, BB, BG, BR, BZ, CA, CN, CO, CR, CU, CZ, DM, DZ, EC, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, OM, PH, PL, RO, SG, SI, SK, TN, TR, TT, UA, US, UZ, VN, YU, ZA					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
IT 2001MI1744	A1	20030210	IT 2001-MI1744		20010809
AU 2002333276	A1	20030224	AU 2002-333276		20020726
PRIORITY APPLN. INFO.:			IT 2001-MI1744	A	20010809
			WO 2002-EP8374	W	20020726

OTHER SOURCE(S): MARPAT 138:163547
AB The invention discloses the use for vasculopathy treatment of nitrooxy compds. (Markush included), or salts thereof. Compds. of the invention include e.g. 2-fluoro-α-methyl-4-diphenylacetic acid (4-nitrooxy)butyl ester (NO-flurbiprofen).
IT 156661-01-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitrooxy compds. for treatment of vasculopaties)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



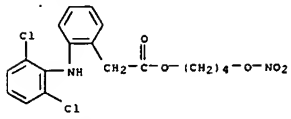
L5 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:736089 CAPLUS
DOCUMENT NUMBER: 137:253012
TITLE: Pharmaceutical compositions containing NO-releasing NSAID and surfactants
INVENTOR(S): Siekmann, Britta; Thoring, Barbro
PATENT ASSIGNEE(S): Astfazeneca AB, Swed.
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

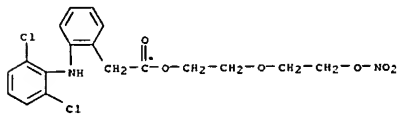
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002074282	A1	20020926	WO 2002-SE476		20020313
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2435825	A1	20020926	CA 2002-2435825		20020313
EP 1370239	A1	20031217	EP 2002-704035		20020313
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
CN 1496253	A	20040512	CN 2002-806527		20020313
BR 2002007760	A	20040601	BR 2002-7760		20020313
JP 2004523577	T	20040805	JP 2002-572990		20020313
ZA 2003006282	A	20041123	ZA 2003-6282		20030813
US 2004096494	A1	20040520	US 2003-471378		20030909
NO 2003004026	A	20031111	NO 2003-4026		20030911
PRIORITY APPLN. INFO.:			SE 2001-901	A	20010315
			WO 2002-SE476	W	20020313

OTHER SOURCE(S): MARPAT 137:253012
AB A new pharmaceutical composition in the form of lipoglobules comprises (a) 1 or more NO-releasing NSAIDs; (b) 1 or more surfactants; and (c) an aqueous phase, and is useful for the treatment of pain and inflammation. Thus, a composition contained 4-(nitrooxy)butyl 6-methoxy-α-methyl-2-naphthaleneacetate 0.77, fractionated coconut oil 2.97, Phospholipon-80 0.76, and Poloxamer-407 1.61 mg/g.
IT 156661-01-7 174454-43-4 311336-64-8 311336-66-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compns. containing NO-releasing NSAID and surfactants)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

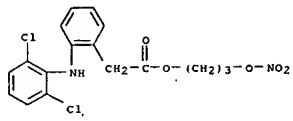
L5 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



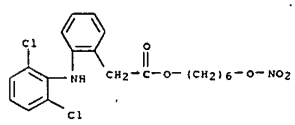
RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



RN 311336-64-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)



RN 311336-66-0 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 6-(nitrooxy)hexyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 11 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:676579 CAPLUS
DOCUMENT NUMBER: 135:231708
TITLE: New self emulsifying drug delivery system
INVENTOR(S): Holmberg, Christina; Siekmann, Britta
PATENT ASSIGNEE(S): AstraZeneca AB, Swed.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

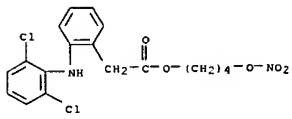
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066088	A1	20010913	WO 2001-SE467	20010306
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2401498	A1	20010913	CA 2001-2401498	20010306
EP 1267832	A1	20030102	EP 2001-910305	20010306
EP 1267832	B1	20040602		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001009014	A	20030603	BR 2001-9014	20010306
JP 2003525894	T	20030902	JP 2001-564741	20010306
HU 200300882	A2	20030929	HU 2003-882	20010306
EE 200200500	A	20040216	EE 2002-500	20010306
AT 268162	T	20040615	AT 2001-910305	20010306
NZ 521009	A	20040625	NZ 2001-521009	20010306
PT 1267832	T	20040930	PT 2001-910305	20010306
ES 2220728	T3	20041216	ES 2001-1910305	20010306
RU 2270675	C2	20060227	RU 2002-122744	20010306
IN 2002MN01102	A	20050304	IN 2002-MN1102	20020816
ZA 2002006740	A	20031124	ZA 2002-6740	20020822
US 2003161846	A1	20030828	US 2002-220791	20020905
NO 2002004272	A	20021105	NO 2002-4272	20020906
HK 1050632	A1	20050318	HK 2003-102781	20030416
PRIORITY APPLN. INFO.:			SE 2000-773 A	20000308
			WO 2001-SE467 W	20010306

OTHER SOURCE(S): MARPAT 135:231708

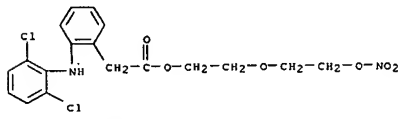
AB The present invention claims and discloses a pharmaceutical composition suitable for oral administration, in form of an emulsion pre-concentrate, comprising: 1 or more NO-releasing NSAID(s), 1 or more surfactants, optionally an addnl. oil or semi-solid fat. The composition forms an in-situ oil-in-water emulsion upon contact with gastrointestinal fluids. The composition may optionally also comprise 1 or more short-chain alcs. Also within the scope of the invention is a combination with a proton pump inhibitor. The pharmaceutical composition is useful in the treatment of pain and inflammation. Further within the scope of the invention is kit comprising a pharmaceutical compn. according to the invention in a unit dosage form, in combination with a proton pump inhibitor, and the proton pump inhibitor is enteric coated. Thus, a semisolid formulation contained a NO-releasing NSAID 750, Pluronic F127 450, and omeprazole 20 g.

IT 156661-01-7 174454-43-4 311336-64-8
311336-66-0
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(self emulsifying drug delivery system)

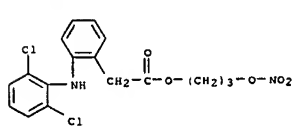
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

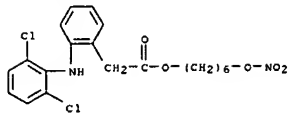


RN 311336-64-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)



RN 311336-66-0 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 6-(nitrooxy)hexyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 12 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L5 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:137173 CAPLUS
DOCUMENT NUMBER: 134:178396
TITLE: Synthesis, activity and formulations of pharmaceutical compounds for treatment of oxidative stress and/or endothelial dysfunction
INVENTOR(S): Del Soldato, Piero
PATENT ASSIGNEE(S): Nicox S.A., Fr.
SOURCE: PCT Int. Appl., 94 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001012584	A2	20010222	WO 2000-EP7225	20000727
WO 2001012584	A3	20020829		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2381409	A1	20010222	CA 2000-2381409	20000727
BR 2000013264	A	20020416	BR 2000-13264	20000727
EP 1252133	A2	20021030	EP 2000-953102	20000727
EP 1252133	B1	20050608		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
HU 200203939	A2	20030328	HU 2002-3939	20000727
JP 2003515526	T	20030507	JP 2001-516885	20000727
NZ 516889	A	20041029	NZ 2000-516889	20000727
AU 781643	B2	20050602	AU 2000-65670	20000727
AT 297375	T	20050615	AT 2000-953102	20000727
EP 1593664	A1	20051109	EP 2005-104064	20000727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, FI, RO, CY				
RU 2264383	C2	20051120	RU 2002-103509	20000727
ES 2243292	T3	20051201	ES 2000-953102	20000727
NZ 535559	A	20051223	NZ 2000-535559	20000727
ZA 2002000628	A	20030423	ZA 2002-628	20020123
NO 2002000623	A	20020409	NO 2002-623	20020208
AU 2005202824	A1	20050721	AU 2005-202824	20050628

PRIORITY APPLN. INFO.: IT 1999-MI1817 A 19990812
EP 2000-953102 A3 20000727
WO 2000-EP7225 W 20000727

OTHER SOURCE(S): MARPAT 134:178396

AB Compds. or their salts of general formula (I): A-B-N(O)s wherein: s is an integer equal to 1 or 2; A = R-T1-, wherein R is the drug radical and T1 =

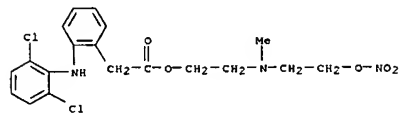
L5 ANSWER 13 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

(CO)t or (X)t', wherein X = O, S, NR1c, R1c is H or a linear or branched alkyl or a free valence, t and t' are integers and equal to zero or 1, with the proviso that t = 1 when t' = 0; t = 0 when t' = 1; B = -TB-X2-O-

wherein TB = (CO) when t = 0, TB = X when t' = 0, X being as above defined; X2, bivalent radical, is such that the precursor drug of A and the precursor of B meet resp. the pharmacol. tests described in the description. Synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction are disclosed. The precursors are such as to meet the pharmacol. test reported in the description.

IT 326850-43-5P
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis, activity and formulations of pharmaceutical compds. for treatment of oxidative stress and/or endothelial dysfunction)

RN 326850-43-5 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[methyl[2-(nitrooxy)ethyl]amino]ethyl ester (9CI) (CA INDEX NAME)



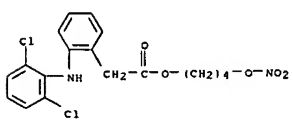
L5 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2002:3642 CAPLUS
DOCUMENT NUMBER: 137:179548
TITLE: Synthesis and anti-inflammatory activity of benzenesulfonylfuroxan-coupled diclofenac
AUTHOR(S): Li, Ruiwen; Zhang, Yihua; Ji, Hui; Yu, Xiaolin; Peng, Sixun
CORPORATE SOURCE: Center of Drug Discovery, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Yaoxue Xuebao (2001), 36(11), 821-826
CODEN: YHHPAL; ISSN: 0513-4870
PUBLISHER: Yaoxue Xuebao Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB New derivs. of diclofenac (DC) having activity of the parent drug and lacking its undesirable effects were screened by coupling DC with NO donor 3,4-dibenzenesulfonylfuroxan through esterification and amidation, evaluating anti-inflammatory activity against xylene-induced mice ear swelling and carrageenan-induced rat paw edema, observing side effects in the rat gastrointestinal tract, and assessing NO releasing ability both in vitro and in vivo. Eleven new compds. I1-11 were synthesized, and their structures were determined by IR, 1HNMR, MS, and elemental anal. Compared with DC, I1-5 and I9 showed no significant difference in anti-inflammatory activity against xylene-induced mice ear swelling. I4 and I5 showed potency comparable to DC in treatment of carrageenan-induced rat paw edema. In GI tract, only slight mucosa surface erosion was found in both I4 and I5 treated rats, while deep ulcer was found in nitrofenac dosed rats and ulcer perforation was found in DC treated rats. Five of eleven rats treated with DC died, one of eight rats treated with nitrofenac died, but no death was found in eight rats dosed with I4 or I5. The detection of occult blood in feces and hematol. index also showed that the extent of GI tract bleeding in I4 and I5 treated rats was much less than that in both DC and nitrofenac treated rats. In addition, I4 and I5 released NO both in vitro and in vivo. Benzenesulfonylfuroxan-coupled DC may possess potency comparable to DC and less GI side effect than DC.

IT 156661-01-7, Nitrofenac
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthesis and anti-inflammatory activity in mice of benzenesulfonylfuroxan-coupled diclofenac)

RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 14 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

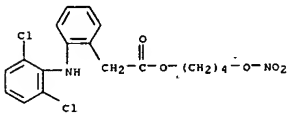
L5 ANSWER 15 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2001:825952 CAPLUS
DOCUMENT NUMBER: 137:88271
TITLE: Pharmacological activity screening of furoxan-coupled diclofenac compounds
AUTHOR(S): Yu, Xiaolin; Ji, Hui; Zhang, Yihua; Li, Ruiwen; Peng, Sixun
CORPORATE SOURCE: Division of Pharmacology, China Pharmaceutical University, Nanjing, 210009, Peop. Rep. China
SOURCE: Zhongguo Yaoke Daxue Xuebao (2001), 32(4), 301-305
CODEN: ZHYXE9; ISSN: 1000-5048
PUBLISHER: Zhongguo Yaoke Daxue
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The relationship in NO-non-steroidal anti-inflammatory drugs between anti-inflammatory activities, gastrointestinal (GI) side effects, and NO release was studied. Two screening models were used to determine the anti-inflammatory effects of the tested furoxan-coupled diclofenac compds.; one was xylene-induced mice ear swelling, and the other was carrageenan-induced rat paw edema. The effects of target compds. on rats' GI system were examined The occult blood in feces was measured and some hematol. indexes (red blood cell count and Hb content) were also determined The NO release in vitro and in vivo was determined Anti-inflammatory activities were increased with the decrease of GI side effects. The GI side effects of all the target compds. with greater anti-inflammatory activities were less than diclofenac and nitrofenac, and NO release in vivo at 3 h was significantly increased. The results showed that the release of NO can resist GI side effects caused by NSAIDs.

IT 156661-01-7, Nitrofenac
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. activity screening of furoxan-coupled diclofenac compds.)

RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2000:861483 CAPLUS
DOCUMENT NUMBER: 134:25340
TITLE: New use of compounds as antibacterial agents
INVENTOR(S): Eek, Arne; Raud, Johan
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072838	A1	20001207	WO 2000-SE1071	20000525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 243672	B	20051121	TW 2000-89109689	20000519
CA 2373653	A1	20001207	CA 2000-2373653	20000525
BR 2000011116	A	20020219	BR 2000-11116	20000525
EP 1196155	A1	20020417	EP 2000-937451	20000525
EP 1196155	B1	20040804		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200103474	T2	20020422	TR 2001-3474	20000525
HU 200201502	A2	20020828	HU 2002-1502	20000525
JP 2003500442	T	20030107	JP 2000-620950	20000525
EE 200100647	A	20030217	EE 2001-647	20000525
NZ 515317	A	20040528	NZ 2000-515317	20000525
AT 272396	T	20040815	AT 2000-937451	20000525
AU 780678	B2	20050407	AU 2000-52623	20000525
RU 2252032	C2	20050520	RU 2001-135826	20000525
US 6593339	B1	20030715	US 2000-673007	20000929
IN 2001MN01424	A	20050304	IN 2001-MN1424	20011115
ZA 2001009497	A	20030217	ZA 2001-9497	20011116
BG 106158	A	20020628	BG 2001-106158	20011128
NO 2001005855	A	20020130	NO 2001-5855	20011130
HK 1045814	A1	20050401	HK 2002-107373	20021009
US 2004048917	A1	20040311	US 2003-426952	20030501
PRIORITY APPLN. INFO.:			SE 1999-2027 A	19990601
			SE 1999-4704 A	19991221
			WO 2000-SE1071 W	20000525
			US 2000-673007 A1	20000929

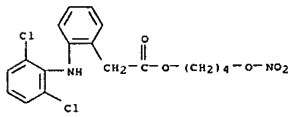
AB The present invention discloses a new use of NO-releasing NSAIDs, especially NO-releasing NSAIDs of formula (I), or a pharmaceutically acceptable salt or enantiomer thereof, for the manufacture of a medicament for the treatment of

L5 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

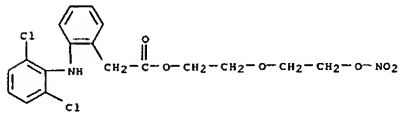
bacterial infections, esp. caused or mediated by Helicobacter pylori. Disclosed is also the new use of a NO-releasing NSAID in combination with an acid susceptible proton pump inhibitor for the treatment of bacterial infections.

IT 156661-01-7 174454-43-4 311336-64-8
311336-66-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of Helicobacter pylori infections with nitric oxide-releasing NSAIDs and proton pump inhibitors)

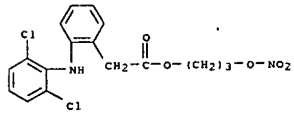
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)

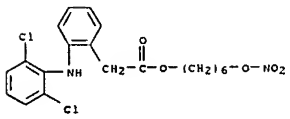


RN 311336-64-8 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 3-(nitrooxy)propyl ester (9CI) (CA INDEX NAME)



RN 311336-66-0 CAPLUS

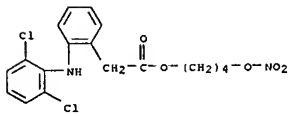
L5 ANSWER 16 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 6-(nitrooxy)hexyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L5 ANSWER 17 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:724578 CAPLUS
DOCUMENT NUMBER: 128:18496
TITLE: Study on paradoxical effects of NSAIDs on platelet activation
AUTHOR(S): Andrioli, Giuseppe; Lussignoli, Sabrina; Gaino, Stefania; Benoni, Giuseppina; Bellavite, Paolo
CORPORATE SOURCE: Inst. Clinical Chem., Univ. Verona, Italy
SOURCE: Inflammation (New York) (1997), 21(5), 519-530
CODEN: INFLD4; ISSN: 0360-3997
PUBLISHER: Plenum
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We recently described a stimulatory effect of high doses (>100 μmol/L) diclofenac on platelet adhesion. In this study we extend our research to the possible biochem. mechanisms of the observed effects, to other non steroidal anti-inflammatory drugs (NSAIDs) (flurbiprofen, indomethacin, acetylsalicylic acid, ibuprofen, nitrofenac and nitroflurbiprofen) and to the effect of high doses diclofenac and flurbiprofen on platelet aggregation. We observed that high doses of diclofenac and of flurbiprofen,
but not of the other tested NSAIDs, increased platelet adhesion at doses ranging from 100 to 500 μmol/L, an effect completely removed by the 12-lipoxygenase-inhibitor nordihydroguaiaretic acid. Moreover, they had no pro-aggregating effect, inhibiting platelet aggregation induced by 10 μmol/L arachidonic acid and dose-dependently increasing the [Ca2+]i. Finally, whereas no basal nitric oxide release by washed platelets was detected, when platelets were incubated by 500 μmol/L diclofenac or flurbiprofen, the production of nitric oxide, as measured by amts. of nitrite
released, was 4.4 ± 0.5 and 3.8 ± 0.4 pmol/5 x 108 platelets/min, resp. Our data indicate that high doses diclofenac and flurbiprofen are promoters of the early phases of platelet activation, probably through the
12-lipoxygenase pathway.
IT 156661-01-7, Nitrofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platelet activation response to nonsteroidal antiinflammatory drugs)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS

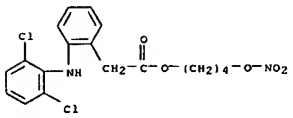
L5 ANSWER 18 OF 33 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 97132990 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8978349
TITLE: Nonsteroidal anti-inflammatory drug enteropathy in rats: role of permeability, bacteria, and enterohepatic circulation.
AUTHOR: Reuter B K; Davies N M; Wallace J L
CORPORATE SOURCE: Intestinal Disease Research Unit, Faculty of Medicine, University of Calgary, Alberta, Canada.
SOURCE: Gastroenterology, (1997 Jan) Vol. 112, No. 1, pp. 109-17.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199701
ENTRY DATE: Entered STN: 19 Feb 1997
Last Updated on STN: 19 Feb 1997
Entered Medline: 21 Jan 1997
AB BACKGROUND & AIMS: The pathogenesis of nonsteroidal anti-inflammatory drug
(NSAID)-induced small intestinal damage remains poorly understood. The aim of this study was to examine the relative importance of the three suggested components of the pathogenesis of NSAID enteropathy, namely, epithelial permeability, enteric bacterial numbers, and enterohepatic recirculation, using an NSAID derivative (nitrofenac) that does not cause small intestinal damage. METHODS: Rats were given diclofenac or nitrofenac at 12-hour intervals. Epithelial permeability to [51Cr]-ethylenediaminetetraacetic acid and enteric bacterial numbers were determined after 1-4 doses of the drugs. Serum levels and biliary excretion of the two drugs were determined by high-performance liquid chromatography. RESULTS: Diclofenac caused a progressive increase in epithelial permeability, marked increases in enteric gram-negative bacterial numbers, and frank intestinal ulceration. Nitrofenac caused similar changes in intestinal permeability after a single dose but no further increase with repeated administration. Moreover, nitrofenac had no effect on enteric bacterial numbers and did not cause frank ulceration.
Unlike diclofenac, nitrofenac did not undergo extensive enterohepatic recirculation. Two other NSAIDs that do not undergo enterohepatic recirculation (nabumetone and aspirin) also did not modify enteric bacterial numbers or cause intestinal ulceration. CONCLUSIONS: Enterohepatic recirculation of NSAIDs is of paramount importance in the pathogenesis of enteropathy caused by these drugs, whereas suppression of prostaglandin synthesis is relatively unimportant.

L5 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:25752 CAPLUS
DOCUMENT NUMBER: 130:231736
TITLE: Nitric oxide as antimicrobial agent "in vivo"
AUTHOR(S): Cuzzolin, Laura; Adami, Alessandra; Crivellente, Federica; Benoni, Giuseppina
CORPORATE SOURCE: Institute of Pharmacology, University of Verona, Verona, Italy
SOURCE: Recent Research Developments in Antimicrobial Agents & Chemotherapy (1997), 2, 95-104
CODEN: RDACFH
PUBLISHER: Research Signpost
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review, with 28 refs. Since nitric oxide is recognized to possess antimicrobial properties and to be a critical mediator of gastrointestinal mucosal defense, in this review the authors report data about the "in vivo" effects of exogenous and endogenous nitric oxide on intestinal microflora and tissue integrity in healthy and inflamed rats. Initially, a model of chronic inflammation (adjuvant arthritis) was used to test the anti-inflammatory efficacy, the gastrointestinal tolerability and the effects on intestinal microflora of nitrofenac, a new NSAID-nitroderivative, in comparison to diclofenac: the results suggest similar therapeutic efficacy of both drugs, a better gastrointestinal tolerability for the new compound and no significant differences between the two drugs about the effects on intestinal microflora. Since it was not possible to correlate the gastrointestinal damage with the bacterial flora changes being the environment modified by the pathol., the role of exogenous nitric oxide, derived from the classical nitric oxide donor sodium nitroprusside, and of the endogenous one, induced by LPS administration, on intestinal flora and on tissue integrity, was investigated in healthy rats. Sodium nitroprusside did not induce any gastrointestinal damage and only partially affected bacterial growth; LPS resulted cytotoxic for all examined aerobic and anaerobic bacteria and induced a moderate jejunal damage. Sodium nitroprusside, when associated to LPS, reverted intestinal damage but not bacterial counts, while L-NAME completely prevented jejunal injury and partially recovered intestinal microflora: this suggest an involvement of an excessive local generation of nitric oxide formed by the inducible NOS enzyme. From this data, it appears evident that the effects of nitric oxide on intestinal bacteria and mucosa are strictly dependent on its concentration in the biol. micro-environment in which nitric oxide is released or present.

IT 156661-01-7, Nitrofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide as in-vivo antimicrobial agent in intestine)

L5 ANSWER 19 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

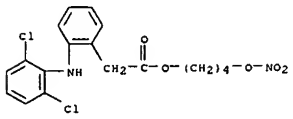
L5 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:63180 CAPLUS
DOCUMENT NUMBER: 128:176060
TITLE: NSAID-induced mucosal injury: Analysis of gastric toxicity of new-generation NSAIDs: ulcerogenicity compared with ulcer healing
AUTHOR(S): Halter, Fred; Rainsford, K. D.; Sirko, Steven P.; Schmassmann, Adrian
CORPORATE SOURCE: Gastrointestinal Unit, Inselspital, University Hospital, Bern, Switz.
SOURCE: Yale Journal of Biology and Medicine (1997), 70(1), 33-43
CODEN: YJBMAU; ISSN: 0044-0086
PUBLISHER: Yale Journal of Biology and Medicine
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some nonsteroidal anti-inflammatory drugs (NSAIDs) delay healing of exptl. gastric ulcers. The 2 exptl. NSAIDs tebufelone and nitrofenac exert relatively low ulcerogenicity in various animal models compared with conventional NSAIDs. In addition, it has been reported that nitrofenac accelerates exptl. acute ulcer healing. The ulcerogenicity of tebufelone was compared with that of indomethacin in arthritic female Lewis rats in a single-dose and a 5-day dosage study. The interference of tebufelone and nitrofenac with ulcer healing was compared with that of indomethacin, diclofenac, omeprazole, and indomethacin plus omeprazole in Wistar rats with gastric cryo-ulcers. The rats were treated for 15 days and ulcer size was sequentially quantified by video endoscopy. Prostanoids in stomach and blood were assessed on day 15. The ulcerogenicity of tebufelone was markedly lower than that of indomethacin at doses with equipotent anti-inflammatory activities. Ulcer healing was accelerated by omeprazole in the 1st wk, but healing was delayed by tebufelone, nitrofenac, indomethacin and diclofenac during the 2nd wk. All the NSAIDs decreased prostanoid synthesis. Overall, tebufelone and nitrofenac delayed gastric ulcer healing to a similar extent as did conventional NSAIDs, even though tebufelone appeared to induce less mucosal damage when determined in standard ulcer assays in rats. Thus, there does not appear to be a relationship between the ulcerogenicity of these NSAIDs and their effect on ulcer healing.

IT 156661-01-7, Nitrofenac
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ulcer formation and healing by)

RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 20 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



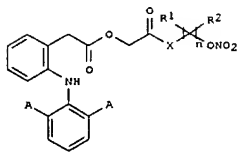
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:681459 CAPLUS
DOCUMENT NUMBER: 125:328304
TITLE: Preparation of nitric esters of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid derivatives
INVENTOR(S): Serra, Masia Xavier; Pi Sallent, Joan
PATENT ASSIGNEE(S): Prodes, S.A., Spain
SOURCE: Eur. Pat. Appl., 16 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 738706	A1	19961023	EP 1996-106009	19960417
EP 738706	B1	19981007		
R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
ES 2092962	A1	19961201	ES 1995-756	19950419
ES 2092962	B1	19970716		
AU 9650428	A	19961031	AU 1996-50428	19960401
AU 683790	B2	19971120		
ZA 9602981	A	19961022	ZA 1996-2981	19960415
CA 2174287	A1	19961020	CA 1996-2174287	19960416
HU 9600996	A2	19961128	HU 1996-996	19960417
CN 1138027	A	19961218	CN 1996-105067	19960417
AT 171936	T	19981015	AT 1996-106009	19960417
NO 9601537	A	19961021	NO 1996-1537	19960418
JP 09020738	A	19970121	JP 1996-98815	19960419
US 5844696	A	19981201	US 1996-634763	19960419
BR 9603235	A	19980428	BR 1996-3235	19960731

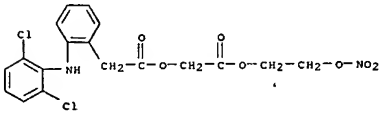
PRIORITY APPLN. INFO.: ES 1995-756 A 19950419

OTHER SOURCE(S): CASREACT 125:328304; MARPAT 125:328304
GI

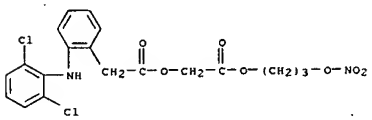


I

L5 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
AB The title compds. [I; A = F, Cl, Br; X = O, NH, NR (R = C1-8 alkyl); R1, R2 = C1-8 alkyl, n = 1-10], potentially useful as antiinflammatory agents (no data), were prepared by condensation of 2-(2,6-dihalophenylamino)phenylacetoxyacetic acid with a compound Y-(C)nR1R2ONO2 [Y = OH, NH2, NHR] in the presence of condensing agent such as N,N'-carbonyldiimidazole in an aprotic organic solvent.
IT 183195-04-2P 183195-06-4P 183195-07-5P
183195-09-7P
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(preparation of nitric esters of 2-(2,6-dihalophenylamino)phenylacetoxyaceti c acid derivs.)
RN 183195-04-2 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

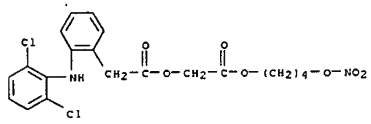


RN 183195-06-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[3-(nitrooxy)propoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

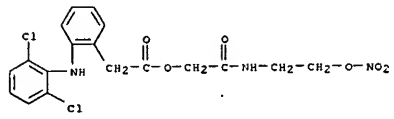


RN 183195-07-5 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[4-(nitrooxy)butoxy]-2-oxoethyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 21 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

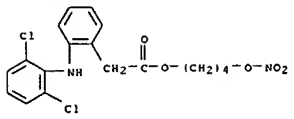


RN 183195-09-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[[2-(nitrooxy)ethyl]amino]-2-oxoethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:253443 CAPLUS
DOCUMENT NUMBER: 124:332273
TITLE: Inhibition of inducible nitric oxide synthase expression by novel nonsteroidal anti-inflammatory derivatives with gastrointestinal-sparing properties
AUTHOR(S): Cirino, G.; Wheeler-Jones, C. P. D.; Wallace, J. L.; Del Soldato, P.; Baydoun, A. R.
CORPORATE SOURCE: Vascular Biology Research Centre, King's College, London, W8 7AH, UK
SOURCE: British Journal of Pharmacology (1996), 117(7), 1421-6
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of novel nitric oxide-releasing nonsteroidal anti-inflammatory compds. (NO-NSAIDs) on induction of nitric oxide (NO) synthase by bacterial lipopolysaccharide (LPS) were examined in a murine cultured macrophage cell line, J774. LPS-induced nitrite production was markedly attenuated by the nitroxybutyl ester derivs. of flurbiprofen (FNBE), aspirin, ketoprofen, diclofenac and ketorolac, with each compound reducing accumulated nitrite levels by >40% at the maximum concns. (100 μg ml-1) used. Further examination revealed that nitrite production was inhibited in a concentration-dependent (1-100 μg ml-1) manner by FNBE which at 100 μg ml-1 decreased LPS stimulated levels by 63.3±8.6% (n=7). The parent compound flurbiprofen was relatively ineffective over the same concentration-range, inhibiting nitrite accumulation by 24±0.9% (n=3) at the maximum concentration used (100 μg ml-1). FNBE reduced LPS-induced nitrite production when added to cells up to 4 h after LPS. Thereafter, FNBE caused very little or no reduction in nitrite levels. Furthermore NO-NSAIDs (100 μg ml-1) did not inhibit the metabolism of L-[3H]-arginine to citrulline by NO synthase isolated from LPS-activated macrophages. Western blot anal. demonstrated that NO synthase expression was markedly attenuated following co-incubation of J774 cell with LPS (1 μg ml-1; 24 h) and FNBE (100μg ml-1; 24 h). Thus taken together, these findings indicate that NO-NSAIDs inhibit induction of NO synthase without directly affecting enzyme activity. In conclusion our results indicate that NO-NSAIDs can inhibit the inducible L-arginine-NO pathway, and are capable of suppressing NO synthesis by inhibiting expression of NO synthase. The clin. implications of these findings remain to be established.
IT 156661-01-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of inducible nitric oxide synthase expression by novel nonsteroidal anti-inflammatory derivs. with gastrointestinal-sparing properties)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)

L5 ANSWER 22 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



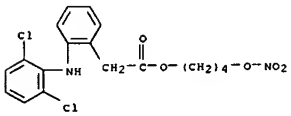
L5 ANSWER 23 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:333513 CAPLUS
DOCUMENT NUMBER: 125:25397
TITLE: Nitric oxide-releasing NSAIDs, a novel class of safe and effective anti-inflammatory agents
AUTHOR(S): Del Soldato, P.; Cuzzolin, L.; Adami, A.; Conforti, A.; Crivellente, F.; Benoni, G.
CORPORATE SOURCE: Policlinico Borgo Roma, University Verona, Verona, 37134, Italy
SOURCE: Inflammopharmacology (1996), 4(2), 181-188
CODEN: IAOAES; ISSN: 0925-4692
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 19 refs. The pharmacotoxicol. profile were reported for three new nitro-anti-inflammatory agents, nitrofenac, nitronaproxen and nitroflurbiprofen with the following results: in models of acute (carrageenan edema) and chronic (adjuvant arthritis) inflammation in the rat, the nitro derivs., compared with the parent drugs, showed similar anti-inflammatory properties by significantly inhibiting both edema volume and arthritis development. The nitroso compds. showed markedly less ulcerogenic activity compared with the parent drugs both in acute conditions and at the end of the chronic inflammation test. The lack of gastrointestinal damage observed with these new anti-inflammatory drugs is the consequence of their ability to release NO. This hypothesis is supported by pharmacokinetic studies and a significant increase in nitrite/nitrate plasma levels.

IT 156661-01-7, Nitrofenac
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nitric oxide-releasing nonsteroidal antiinflammatory agents)

RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:258954 CAPLUS
DOCUMENT NUMBER: 124:332445
TITLE: Effects of a new class of NO-releasing NSAIDs on platelets and isolated arteries
AUTHOR(S): Minuz, P.; Lechi, C.; Bonapace, S.; Gaino, S.; Adami, A.; Cuzzolin, L.; Del Soldato, P.; Benoni, G.
CORPORATE SOURCE: Istituto di Clinica Medica, University Verona, Italy
SOURCE: Inflammopharmacology (1996), 4(1), 83-90
CODEN: IAOAES; ISSN: 0925-4692
PUBLISHER: Kluwer
DOCUMENT TYPE: Journal
LANGUAGE: English

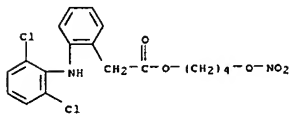
AB A new class of nitro derivs. of nonsteroidal anti-inflammatory drugs has recently been synthesized (Nicox Ltd., London, UK). In order to improve gastric tolerance of the parent compound, a side-chain, able to release nitric oxide, has been added to the core structure of the mol. We studied in vitro the effects of nitrofenac and two NO-aspirins (NCX 4215 and NCX 4016) on platelets and isolated arteries to identify any possible effect due to the release of nitric oxide or to the inhibition of cyclooxygenase activity. Nitrofenac induced a dose-dependent relaxation both with intact (46% with 1 + 10-3 mol/L) and endothelium-denuded (75% with 1 + 10-3 mol/L) rings of rat aorta precontracted with epinephrine, while diclofenac did not affect this contraction (0% relaxation in intact and 22% in rubbed arteries). Pretreatment with diclofenac 1 + 10-3 mol/L significantly increased the vasorelaxant effects of nitrofenac at each drug concentration, both in intact (86% with 1 + 10-3 mol/L) and rubbed prepns. (89%). NO-aspirins, unlike acetylsalicylic acid, were able to relax both intact and endothelium-denuded rings of rat aorta (100% relaxation). Methylene blue and oxyHb completely reversed the relaxation induced by nitrofenac and NO-aspirins, both in rubbed and intact aortic rings. Both NO-aspirins exhibited antiaggregating properties in arachidonic acid-stimulated human platelets, measured using a turbidimetric method (NCX 4215, 1 + 10-3 mol/L: 70% inhibition; NCX 4016, 1 + 10-4 mol/L: 100%), NCX 4016 proving as effective as acetylsalicylic acid 1 + 10-5 mol/L. Thrombin-induced platelet aggregation was inhibited in acetylsalicylic acid-treated platelets (NCX 4215, 1 + 10-3 mol/L: 50%, NCX 4016, 1 + 10-4 mol/L: 92%). NCX 4016 was also able to prevent thrombin-induced intracellular free calcium increase, an effect not observed with acetylsalicylic acid. In vitro thromboxane A2 production in human platelets, assayed by RIA as thromboxane B2 serum concentration, was reduced by NCX 4215, 1 + 10-3 mol/L (76%) and virtually abolished by NCX 4016 5 + 10-5 mol/L (95% inhibition). These results demonstrate in vitro the antiaggregating activity of NO-aspirins, NCX 4016 being more active than NCX 4215, and the vasorelaxant effects of all the tested mols. The mechanism involved is two-fold: release of nitric oxide and inhibition of cyclooxygenase.

IT 156661-01-7, Nitrofenac
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NO-releasing NSAID effect on platelets and isolated arteries)

RN 156661-01-7 CAPLUS

L5 ANSWER 24 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



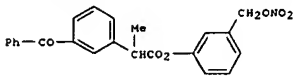
L5 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:163887 CAPLUS
DOCUMENT NUMBER: 124:201789
TITLE: Preparation of aryl nitrate ester compounds having antiinflammatory ans well as analgesic and antithrombotic activities
INVENTOR(S): Del Soldato, Piero; Sannicolo', Francesco
PATENT ASSIGNEE(S): Nicox Ltd., Ire.
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9530641	A1	19951116	WO 1995-EP1233	19950404
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2190087	C	19951116	CA 1995-2190087	19950404
CA 2190087	A1	19951116		
AU 9522156	A	19951129	AU 1995-22156	19950404
AU 702662	B2	19990225		
EP 759899	A1	19970305	EP 1995-915185	19950404
EP 759899	B1	19990915		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, NL, PT, SE				
HU 75961	A2	19970528	HU 1996-3107	19950404
BR 9507634	A	19970923	BR 1995-7634	19950404
JP 09512798	T	19971222	JP 1995-528615	19950404
AT 184589	T	19991015	AT 1995-915185	19950404
ES 2139199	T3	20000201	ES 1995-915185	19950404
RU 2145595	C1	20000220	RU 1996-123280	19950404
US 5861426	A	19990119	US 1997-737426	19970306
US 5780495	A	19980714	US 1997-902570	19970729
GR 3032078	T3	20000331	GR 1999-403169	19991208

PRIORITY APPLN. INFO.:	IT 1994-MI916	A	19940510
	IT 1994-MI1731	A	19940809
	GB 1993-20599	A	19931006
	WO 1995-EP1233	W	19950404
	US 1996-624508	A3	19960405

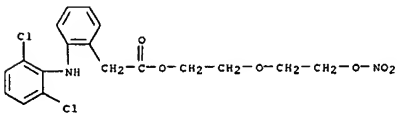
OTHER SOURCE(S): MARPAT 124:201789
GI

L5 ANSWER 25 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



I

AB The title compds. AX1NO2 [A = R(COXu)t; t = 0, 1; u = 0, 1; X = O, (un)substituted NH or NR1c wherein R1c = alkyl; R = (un)substituted Ph, etc.; X = YO; Y = alkylene, cycloalkylene, oxyalkyl, etc.] (e.g., I), which inhibit cyclooxygenase, are prepared
IT 174454-43-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aryl nitrate ester compds. having antiinflammatory ans well as analgesic and antithrombotic activities)
RN 174454-43-4 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 2-[2-(nitrooxy)ethoxy]ethyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 26 OF 33 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 95340109 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7615202
TITLE: A nitric oxide-releasing nonsteroidal anti-inflammatory drug accelerates gastric ulcer healing in rats.
AUTHOR: Elliott S N; McKnight W; Cirino G; Wallace J L
CORPORATE SOURCE: Intestinal Disease Research Unit, University of Calgary, Alberta, Canada.
SOURCE: Gastroenterology, (1995 Aug) Vol. 109, No. 2, pp. 524-30.
Journal code: 0374630. ISSN: 0016-5085.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 5 Sep 1995
Last Updated on STN: 5 Sep 1995
Entered Medline: 22 Aug 1995

AB BACKGROUND & AIMS: Nonsteroidal anti-inflammatory drugs (NSAIDs) have well-characterized inhibitory effects on gastric ulcer healing. A new class of gastrointestinal-sparing, nitric oxide-releasing NSAID derivatives has been recently described. This study was performed to determine if one of these compounds (nitrofenac) would influence healing of a preexisting ulcer. METHODS: Seven days after induction of gastric ulcer with serosal acetic acid, daily oral treatment with antiinflammatory doses of diclofenac, nitrofenac, or vehicle was started. After 7 days of treatment, the ulcer area was measured. The effects of misoprostol and two drugs that show in vitro selectivity for inhibiting cyclooxygenase 2 (nabumetone and L745,337) were also assessed. RESULTS: Diclofenac, nabumetone, and L745,337 had no effect on ulcer healing when compared with vehicle. Only diclofenac significantly decreased hematocrit and weight gain. On the other hand, nitrofenac significantly accelerated healing. Glyceryl trinitrate also significantly and dose dependently accelerated healing. Nitrofenac suppressed cyclooxygenase 1 activity to a similar extent as diclofenac. CONCLUSIONS: These results show that an NO-releasing NSAID derivative and an NO donor could accelerate ulcer healing, whereas a standard NSAID, misoprostol, and two inhibitors of cyclooxygenase 2 had no effect. In addition to sparing the gastrointestinal tract, NO-releasing NSAIDs, despite suppressing cyclooxygenase activity, are capable of accelerating tissue repair.

L5 ANSWER 27 OF 33 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 95335361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7610982
TITLE: Nitric oxide-releasing NSAIDs: a novel class of GI-sparing anti-inflammatory drugs.
AUTHOR: Wallace J L; Pitman O J; Cirino G
CORPORATE SOURCE: Department of Pharmacology & Therapeutics, University of Calgary, Alberta, Canada.
SOURCE: Agents and actions. Supplements, (1995) Vol. 46, pp. 121-9.
Journal code: 7801014. ISSN: 0379-0363.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199508
ENTRY DATE: Entered STN: 28 Aug 1995
Last Updated on STN: 28 Aug 1995
Entered Medline: 17 Aug 1995

AB The addition of a nitric oxide-releasing moiety to a number of common nonsteroidal anti-inflammatory drugs markedly reduces their toxicity in the gastrointestinal tract without interfering with their ability to inhibit prostaglandin synthesis. Moreover, the anti-inflammatory and anti-pyretic activities of the nitric-oxide releasing NSAID were comparable to the parent compound, while the anti-thrombotic activity in vivo was significantly enhanced. Nitric oxide-releasing NSAIDs may represent an alternative to existing anti-inflammatory, anti-pyretic and anti-thrombotic agents with greatly reduced toxicity in the gastrointestinal tract.

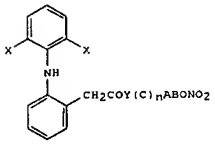
L5 ANSWER 28 OF 33 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 95230523 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7714752
TITLE: Plasma concentrations and pharmacokinetic parameters of nitrofenac using a simple and sensitive HPLC method.
AUTHOR: Benoni G; Terzi M; Adami A; Grigolini L; Del Soldato P; Cuzzolin L
CORPORATE SOURCE: Institute of Pharmacology, University of Verona, Policlinico Borgo Roma, Italy.
SOURCE: Journal of pharmaceutical sciences, (1995 Jan) Vol. 84, No. 1, pp. 93-5.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 24 May 1995
Last Updated on STN: 24 May 1995
Entered Medline: 18 May 1995

AB An accurate and sensitive HPLC method has been developed for the determination of nitrofenac, a new, original diclofenac derivate showing a good tolerability and a wide anti-inflammatory profile, diclofenac, and its metabolites in plasma. This method has been applied to evaluate the pharmacokinetic parameters of the drugs, using a noncompartmental model, after the oral administration of 5 mg/kg nitrofenac to rats. Nitrofenac and the internal standard flufenamic acid were dissolved in acetonitrile, and diclofenac was dissolved in methanol. The drugs were eluted from a 5 microns LC-8 column with a mobile phase consisting of acetonitrile/water (50/50 v/v) adjusted to pH 3.3 with glacial acetic acid, at a flow rate of 2 mL/min with UV detection at 280 nm for diclofenac and 275 nm for nitrofenac. The detection limit for the drugs in plasma was 25 ng/mL. The peak concentration of nitrofenac was reached 7 h after drug administration, while with diclofenac we observed three peaks at 2, 5, and 10 h; the mean residence time and the elimination rate constant for nitrofenac were 6.18 +/- 0.09 h and 0.37 +/- 0.03 h-1 respectively, while those for diclofenac were 12.24 +/- 0.11 h and 0.11 +/- 0.04 h-1. Under our conditions, the metabolism of nitrofenac produced 23% diclofenac and other metabolites: the plasma concentrations and kinetic characteristics of diclofenac are enough to induce an anti-inflammatory activity, while the clinical importance of the other metabolites remains to be elucidated.

L5 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:508221 CAPLUS
DOCUMENT NUMBER: 121:108221
TITLE: Nitric esters of derivatives of 2-(2,6-di-halophenylamino)phenylacetic acid and process for their preparation
INVENTOR(S): Matji, Jose Antonio; Alcaide, Antonio
PATENT ASSIGNEE(S): Corlay S. L., Spain; Metgrove Ltd.
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9404484	A1	19940303	WO 1993-EP1906	19930720
W: BR, CA, JP, KR, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 609415	A1	19940810	EP 1993-917596	19930720
EP 609415	B1	19961009		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07500355	T	19950112	JP 1993-505826	19930720
AT 143941	T	19961015	AT 1993-917596	19930720
ES 2093979	T3	19970101	ES 1993-917596	19930720
RU 2109009	C1	19980420	RU 1994-46148	19930720
JP 3231042	B2	20011119	JP 1994-505826	19930720
CA 2120942	C	20050927	CA 1993-2120942	19930720
US 5597847	A	19970128	US 1994-211447	19940331
PRIORITY APPLN. INFO.:			IT 1992-MI2006 A	19920820
			WO 1993-EP1906 W	19930720

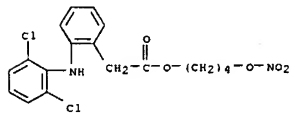
OTHER SOURCE(S): CASREACT 121:108221; MARPAT 121:108221
GI



I

AB Title compds. I (A, B = H, alkyl; X Br, Cl; Y = O, HN, R1N wherein R1 = alkyl; n = 1-10) useful as analgesics and antiinflammatories, and for treatment of immunol. disorders, cardiovascular, myocardial and brain

L5 ANSWER 29 OF 33 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
ischemia and arterial thrombosis (data given for the 1st 2 disorders), are prepd. by a process consisting of a limited no. of phases, satisfactory yields and high amts. even on an industrial basis. Br(CH2)4Cl in DMF was added to Na 2-[(2,6-dichlorophenyl)amino]phenylacetate in DMF to give the 4-chlorobutyl ester which was treated with AgNO3 in MeCN to give I (A = B = H, X = Cl, Y = O, n = 4). Analgesic and antiinflammatory activities for I were shown.
IT 156661-01-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as analgesic and antiinflammatory)
RN 156661-01-7 CAPLUS
CN Benzeneacetic acid, 2-[(2,6-dichlorophenyl)amino]-, 4-(nitrooxy)butyl ester (9CI) (CA INDEX NAME)



L5 ANSWER 30 OF 33 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 94374449 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8088345
TITLE: A diclofenac derivative without ulcerogenic properties.
AUTHOR: Wallace J L; Reuter B; Cicala C; McKnight W; Grisham M; Cirino G
CORPORATE SOURCE: Gastrointestinal Research Group, Faculty of Medicine, University of Calgary, Alberta, Canada.
SOURCE: European journal of pharmacology, (1994 May 23) Vol. 257, No. 3, pp. 249-55.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199410
ENTRY DATE: Entered STN: 31 Oct 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 18 Oct 1994

AB In this study, we assessed the effects of addition of a nitroxybutyl moiety to diclofenac on its ulcerogenic properties. The diclofenac derivative, 'nitrofenac', was examined in terms of its ability to induce acute gastric erosions and chronic-type gastric ulcers in rats and rabbits, respectively. The effects of these compounds on prostaglandin synthesis in the stomach and at a site of peripheral inflammation were also assessed, as were their anti-inflammatory properties in a model of acute inflammation. Diclofenac dose-dependently caused acute gastric mucosal injury in the rat at all doses tested (10-40 mg/kg), that was significantly greater in severity than that observed with the same doses of nitrofenac. In rabbits, twice-daily administration of diclofenac induced penetrating antral ulcers and small intestinal damage. No damage was observed in the stomach or small intestine of rabbits receiving nitrofenac. Diclofenac and nitrofenac exerted similar inhibitory effects on prostaglandin E2 synthesis in the stomach and in a carrageenan-sponge model of peripheral inflammation. These compounds exerted similar inhibitory effects on carrageenan-induced paw edema. Nitrofenac, but not diclofenac, caused a significant increase in plasma levels of nitrate/nitrite. These results suggest that the addition of a nitroxybutyl moiety to diclofenac markedly reduces the ulcerogenic properties of this compound without interfering with its ability to inhibit cyclo-oxygenase activity or to reduce acute inflammation.

L5 ANSWER 31 OF 33 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 94261529 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8202446
TITLE: Effects on intestinal microflora, gastrointestinal tolerability and antiinflammatory efficacy of diclofenac and nitrofenac in adjuvant arthritic rats.
AUTHOR: Cuzzolin L; Conforti A; Donini M; Adami A; Del Soldato P; Benoni G
CORPORATE SOURCE: Institute of Pharmacology, University of Verona, Italy.
SOURCE: Pharmacological research : the official journal of the Italian Pharmacological Society, (1994 Jan-Feb) Vol. 29, No. 1, pp. 89-97.
Journal code: 8907422. ISSN: 1043-6618.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 14 Jul 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 7 Jul 1994

AB Since it is known that nitric oxide plays an important protective role in maintaining the tissue integrity and is cytotoxic for invasive micro-organisms, diclofenac and a new original diclofenac-derivate, nitrofenac (containing the nitric oxide group), was administered at doses of 0.3 and 3 mg kg-1 per os to adjuvant arthritic rats. At the 14th, 21st and 28th days after arthritis induction, the antiinflammatory efficacy and the effects on intestinal microflora of the two drugs were evaluated; moreover, at the end of the study period, the gastrointestinal tract was examined macroscopically for any presence of lesions. Daily oral administration of diclofenac and nitrofenac at 3 mg kg-1 markedly and significantly inhibited arthritis development until the end of the study period. Some significant changes were observed in anaerobic and Gram-negative bacterial flora, particularly the total disappearance, in all treated rats, of Escherichia coli 1, also 7 days after the last drug administration. Finally, no ulcers or severe damage were observed macroscopically with either drug, even if some alterations in the mucosa and haemorrhagic effusions were more evident in rats treated with diclofenac at 3 mg kg-1. In conclusion, in this chronic model a similar therapeutic efficacy of diclofenac and nitrofenac is shown in arthritic rats. The better gastrointestinal tolerability observed in nitrofenac-treated rats could be attributed to the release of nitric oxide.

L5 ANSWER 32 OF 33 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 94285693 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8015340
TITLE: Markedly reduced intestinal toxicity of a diclofenac derivative.
AUTHOR: Reuter B K; Cirino G; Wallace J L
CORPORATE SOURCE: Gastrointestinal Research Group, University of Calgary, Alberta, Canada.
SOURCE: Life sciences, (1994) Vol. 55, No. 1, pp. PL1-8.
Journal code: 0375521. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 10 Aug 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 25 Jul 1994

AB Addition of a nitroxybutyl moiety to diclofenac greatly reduces its damaging effects on the gastric mucosa without altering its ability to suppress prostaglandin synthesis and exert anti-inflammatory actions. The present study was performed in order to determine if this derivative of diclofenac, called nitrofenac, would also have less toxicity in the small and large intestine when administered repeatedly over a 1-2 week period. Healthy rats were given equimolar doses of diclofenac (10 mg/kg) or nitrofenac (15 mg/kg) twice daily for up to two weeks. All 10 rats receiving diclofenac died prior to completion of the study, exhibiting massive small intestinal ulceration and perforation. No deaths were observed in the rats treated with nitrofenac, and the only small intestinal abnormality observed was diffuse hyperemia. As nonsteroidal anti-inflammatory drugs have been shown to exacerbate colitis, we compared the effects of twice daily treatment with diclofenac (1-10 mg/kg) or nitrofenac (1.5-15 mg/kg) for 1 week in rats in which colitis had been induced with trinitrobenzene sulfonic acid. Diclofenac administration resulted in mortality which increased dose-dependently (e.g. 86% at 5 mg/kg) and was associated with perforation of the colon. Mortality was not observed with nitrofenac at doses of 1.5 or 7.5 mg/kg, while at 15 mg/kg the mortality rate was 33%. None of the doses of nitrofenac significantly augmented colonic injury or granulocyte infiltration (measured by myeloperoxidase activity). Suppression of colonic prostaglandin E2 synthesis was comparable with equimolar doses of diclofenac and nitrofenace. These studies demonstrate that nitrofenac has markedly reduced intestinal toxicity in healthy and colitic rats when compared to diclofenac.

L5 ANSWER 33 OF 33 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 94295465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8023740
TITLE: Acute anti-inflammatory activity and gastrointestinal tolerability of diclofenac and nitrofenac.
AUTHOR: Conforti A; Donini M; Brocco G; Del Soldato P; Benoni G; Cuzzolin L
CORPORATE SOURCE: Institute of Pharmacology, University of Verona, Italy.
SOURCE: Agents and actions, (1993 Nov) Vol. 40, No. 3-4, pp. 176-80.
Journal code: 0213341. ISSN: 0065-4299.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 15 Aug 1994
Last Updated on STN: 29 Jan 1996
Entered Medline: 29 Jul 1994

AB Diclofenac and its derivative nitrofenac were compared to test their anti-inflammatory efficacy and gastrointestinal toxicity in rats. A similar good anti-inflammatory activity of the two drugs was observed in carrageenan oedema and a marked gastrointestinal toxicity was induced by diclofenac, while nitrofenac failed to produce gastric damage even with very high doses (50 and 100 mg/kg). The lack of the gastric ulcers in rats treated with nitrofenac could be due to the absorption of the drug as an inactive inhibitor of PG synthesis and/or to the fact that probably nitric oxide is released in the intestine and plays an important protective role in maintaining the tissue integrity.

=> log h

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	134.65	307.41

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-19.50	-19.50

SESSION WILL BE HELD FOR 120 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 11:30:07 ON 19 JAN 2007